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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/734,570	12/12/2003	Youcef M. Rustum	03551.0145	1870

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EXAMINER	
GRAFFEO, MICHELLE	
ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 07/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/734,570	RUSTUM ET AL.	
	Examiner	Art Unit	
	Michelle Graffeo	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-12 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-12 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 5/26/04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S.O.O

DETAILED ACTION

Status of Action

Claims 1-12 are pending and examined.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spasic et al. The Role of Selenium supplementation on Attenuation of Toxic Doxorubicin Effects. Naucni Skupovi-Srpska Akademiji Nauka I Umetnosti, Odeljenje Prirodno-Matematickih Nauka (1995), 6(Conference on Selenium-1993), 119-130. taken with Dong et al., Protective Effects of Selenium Supplementation in Minimizing 5-Fluorouracil Induced Lipid Peroxidative Damage of the Small Intestine. The Journal of Trace Elements in Experimental Medicine 10:163-171 (1997) further in view of US Patent Application No. 20010044431 to Rodriguez.

Spasic et al. teach that pretreatment with a selenium compound can attenuate the toxic effects of doxorubicin on several tissue types (see Abstract and Discussion on page 124).

Spasic et al. do not recite the use of seleno-L-methionine or methylselenocysteine in particular or the use of the anticancer agent oxaliplatin. Neither does Spasic et al. teach that higher than therapeutic doses of oxaliplatin or doxorubicin can be administered due to the protective effects of selenium.

Dong et al. teach that dietary supplementation of selenium can minimize the damage of 5-fluorouracil in the small intestine in rats (see Abstract and discussion on page 167) by adding selenium to the diet via drinking water for 5 weeks prior to dosing of 5-fluorouracil (see materials and methods page 164). Dong et al. do not specifically teach that selenium compounds can have such protective effects with other chemotherapies, but do state that "5-FU, like other anticancer drugs, also can induce lipid peroxidative damage. This was the toxic consequence of a chemical insult and

unrelated to the structure of the drug." Therefore, one skilled in the art would find it obvious to substitute a standard chemotherapy such as oxaliplatin in this reference.

Rodriguez teaches that selenium compounds can be employed to treat ovarian cancer (see paragraph 25). Selenium compounds mentioned in Rodriguez include selenomethionine (see paragraph 160) and methylselenocysteine (see paragraph 162). As reported herein, selenomethionine is preferred because of its commercial availability and anticancer effects. Se-methylselenocysteine is reported herein to be of equal or greater value than selenomethionine in cancer prevention because it has been shown to induce cell death by apoptosis.

Furthermore, the antineoplastic properties of selenium are known and would motivate one skilled in the art to routinely optimize the dose regimes depending upon the desired results to the extent that the dose is non-toxic. Similarly, one skilled in the art would as part of routine treatment, optimize patient specific dosages of anticancer agents such as doxorubicin and thus routinely administer an agent such as doxorubicin at higher levels upon concurrent or sequential administration with a selenium compound.

One skilled in the art would be motivated to combine Spasic et al. with Dong et al. and Rodriguez. All references are directed to the use of selenium compounds in the treatment of cancer. Dong et al. teach that other anticancer agents are toxic via the same mechanism as 5-FU which suggests that selenium would be effective in attenuating the toxic effects of various other chemotherapies, as is confirmed by the teachings in Spasic et al. Rodriguez names the specific selenium compounds that are

used in the treatment of cancer as part of a multivalent cancer therapy (see paragraphs 16-17 which discuss other agents such as those which promote apoptosis for example). Thus, the claimed invention of the method was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 7-12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 16-19 of copending Application No. 10/844800 in view Dong et al., Protective Effects of Selenium Supplementation in Minimizing 5-Fluorouracil Induced Lipid Peroxidative Damage of the Small Intestine. The Journal of Trace Elements in Experimental Medicine 10:163-171 (1997) as applied above.

The '800 Application claims a method for using taxotere at a higher than therapeutic dose comprising administering the taxotere and a selenium compound

wherein the toxicity of taxotere is reduced with the administration of the selenium compound. The '800 Application further claims a selenium compound which is seleno-L-methionine or methylselenocysteine and a method wherein the selenium compoundis administered at a time selected from prior to, during or following the administration of taxotere.

The '800 Application does not claim a method of using oxaliplatin or doxorubicin at higher than therapeutic doses along with a selenium compound.

As discussed above, Dong et al. state that "5-FU, like other anticancer drugs, also can induce lipid peroxidative damage. This was the toxic consequence of a chemical insult and unrelated to the structure of the drug." Therefore, one skilled in the art would find it obvious to substitute a standard chemotherapy such as oxaliplatin or doxorubicin in this reference. The substitution of doxorubicin is further confirmed by Spasic et al. which as also discussed above, teach that pretreatment with a selenium compound can attenuate the toxic effects of doxorubicin on several tissue types.

This is a provisional obviousness-type double patenting rejection.

No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Graffeo whose telephone number is 571-272-8505. The examiner can normally be reached on 9am to 5:30pm Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

5 Jul 2005
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